This application is a continuation of co-pending USSN 09/291,406, filed April 13, 1999, now U.S. Patent No. 6,270,954 B1, which is a continuation in part of USSN 08/838,691, filed April 9, 1997, now U.S. Patent No. 5,900,360, which claims priority to U.S. provisional application no. 60/015,155, filed April 10, 1996 all of which are incorporated by reference for all purposes. The government may own certain rights in the present invention pursuant to grants from the Cystic Fibrosis Foundation (R613) and NIH (AG-10770).

IN THE CLAIMS:

Please delete currently pending claims 1-22 and add the following new claims 23-34:

--23. (New) A method of improving a phenotypic defect in a mammalian cell that contains a conformationally defective target protein wherein the conformational defect causes the phenotypic defect, comprising contacting a first cell that expresses said conformationally defective target protein with an amount of a protein stabilizing agent that is effective to improve the conformational defect, thereby improving the phenotypic defect of the first cell in comparison with a second cell having the same conformationally defective target protein and phenotypic defect, wherein the second cell is not contacted with the protein stabilizing agent, with the proviso that the protein stabilizing agent is not congo red, DMSO or glycerol.

24. (New) The method according to claim 23, wherein the defective target protein is the gene product of a naturally occurring mutant nucleic acid.

25. (New) The method according to claim 23, wherein the defective target protein is the gene product of a heterologous nucleic acid.

26. (New) The method according to claim 23, wherein the defective target protein is selected from the group consisting of the cystic fibrosis transmembrane conductance regulator (CFTR) protein, emphysema and chronic liver disease α-1 anti-trypsin inhibitor, LDL receptor (familial hypercholesterolinemia), β-hexylaminidase (Tay-sachs), fibrillin (Marfan syndrome) superoxide dismutase (amyotropic lateral sclerosis), collagen (scurvy), α-ketoacid dehydrogenase complex (maple syrup urine disease), p53 (cancer), type I procollagen pro-α (osteogenesis

imperfecta), β-amyloid (Alzheimer's disease), crystallins (cataracts), rhodopsin (retinitis pigmentosa), and insulin receptor (leprechaunism).

5 ~~27.~~ (New) The method according to claim 1 ~~23~~, wherein the protein stabilizing agent is selected from the group consisting of deuterated water, polyols and sugars, including erythritol, inositol, trehalose isofluoroside, polyethylene glycol, amino acids and derivatives thereof, including glycine, alanine, proline, taurine, betaine, octopine, glutamate, sarcosine, gamma-aminobutyric acid, and trimethylamine N-oxide (TMAO).

6 ~~28.~~ (New) The method according to claim 1 ~~23~~, wherein the phenotypic defect is caused by a condition selected from the group consisting of improper folding, improper co- and post-translational modification, improper subcellular targeting, inability to bind biological ligands, aggregation, proteolytic degradation, temperature sensitive folding, and any combination thereof.

A2 cont'd

7 ~~29.~~ (New) The method according to claim 6 ~~28~~, wherein the condition that causes the phenotypic defect occurs in a part of the protein that is selected from the group consisting of pre-sequence, pro-sequence, and mature protein sequence.

8 ~~30.~~ (New) A method of improving a phenotypic defect in a mammalian cell that contains a conformationally defective target protein wherein the conformational defect causes the phenotypic defect, and wherein the conformational defect is a temperature sensitive folding defect, comprising contacting a first cell that expresses said conformationally defective target protein with an amount of a protein stabilizing agent that is effective to improve the conformational defect, thereby improving the phenotypic defect of the first cell in comparison with a second cell having the same conformationally defective target protein and phenotypic defect, wherein the second cell is not contacted with the protein stabilizing agent, with the proviso that the protein stabilizing agent is not congo red, DMSO or glycerol.

9 ~~31.~~ (New) A method of improving a phenotypic defect in a mammalian cell that contains a conformationally defective target protein wherein the

A

conformational defect causes the phenotypic defect, and wherein the defective target protein is an enzyme, comprising contacting a first cell that expresses said conformationally defective target protein with an amount of a protein stabilizing agent that is effective to improve the conformational defect, thereby improving the phenotypic defect of the first cell in comparison with a second cell having the same conformationally defective target protein and phenotypic defect, wherein the second cell is not contacted with the protein stabilizing agent, with the proviso that the protein stabilizing agent is not congo red, DMSO or glycerol.

10
~~32.~~ (New) A method of improving a phenotypic defect in a mammalian cell that contains a conformationally defective target protein wherein the conformational defect causes the phenotypic defect, and wherein the conformational defect causes improper protein targeting, comprising contacting a first cell that expresses said conformationally defective target protein with an amount of a protein stabilizing agent that is effective to improve the conformational defect, thereby improving the phenotypic defect of the first cell in comparison with a second cell having the same conformationally defective target protein and phenotypic defect, wherein the second cell is not contacted with the protein stabilizing agent, with the proviso that the protein stabilizing agent is not congo red, DMSO or glycerol.

A2 cont'd

11
~~33.~~ (New) A method of improving a phenotypic defect in a mammalian cell that contains a conformationally defective target protein wherein the conformational defect causes the phenotypic defect, comprising contacting a first cell that expresses said conformationally defective target protein with an amount of a protein stabilizing agent that is effective to improve the conformational defect, thereby improving the phenotypic defect of the first cell in comparison with a second cell having the same conformationally defective target protein and phenotypic defect, wherein the second cell is not contacted with the protein stabilizing agent, and wherein the protein stabilizing agent is trimethylamine N-oxide.

12
~~34.~~ (New) A method of improving a phenotypic defect in a mammalian cell that contains a conformationally defective target protein wherein the

A